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Drug likeness prediction of 5-hydroxy-substituted coumarins with high affinity to 5-HT_{1A} and 5-HT_{2A} receptors

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ABSTRACT

One of the latest trends is search for the new anti-psychotic drugs among coumarin derivatives with piperazine moiety. Their therapeutic potential can be hampered by poor physico-chemical parameters as low brain penetration or limited transport in the body fluid. Herein, we predicted the drug likeness of six coumarins with high affinity towards 5-HT_{1A} and 5-HT_{2A} receptors. Subsequent experimental determination of their binding constants to human serum albumin (HSA) revealed the binding with a moderate strength (logK = 4.8 – 5.8) at the Sudlow's site 1, which represents a possibility of temporary storage of tested coumarins on HSA. Computational mapping of the binding of coumarins - HSA complexes showed that the coumarin rings of all tested compounds were similarly located within the hydrophobic binding pocket of HSA, while the rest of molecules (composed with alkyl chains, piperazine and benzene rings)